Comments of the Council for Education and Research on Toxics (CERT)

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Acrylamide

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Agency	Abbrev.	Rank	Classification
International Agency for Research on Cancer	IARC	2A	Probably carcinogenic to humans
National Toxicology Program	NTP	-------	Reasonably anticipated to be a human carcinogen
Environmental Protection Agency	EPA	B2	Probable human carcinogen
Health Council of Netherlands	HCN	2	Should be regarded as carcinogenic to humans
Office of Environmental Health Hazard Assessment	OEHHA	-------	Known to the State of California to cause cancer

Acrylamide

- Basis of IARC Classification: sufficient evidence in animals and supportive evidence of genotoxicity: acrylamide and glycidamide induce hemoglobin and DNA adducts, acrylamide induces gene mutations and chromosome aberrations (clastogenicity)
- A multi-site carcinogen, producing tumors in multiple organs in multiple species of animals
- The World Health Organization (WHO) has concluded that acrylamide in food is a “major concern” for human health.

Acrylamide

- Acrylamide is a potent carcinogen.
- Based on data from the US-EPA Integrated Risk Information System (IRIS), OEHHA calculated a Safe Harbor Level of 0.2 micrograms per day.
- This is a very low level of exposure; acrylamide is a more potent carcinogen than such familiar known human carcinogens as benzene and formaldehyde.

Acrylamide

- In 2002 Swedish researchers discovered that acrylamide is present in various cooked foods.
- Shortly thereafter scientists showed that acrylamide is formed when foods that contain asparagine and reducing sugars are cooked at high temperatures .
- Acrylamide is formed via the Maillard reaction – the “browning” reaction that occurs when food is cooked.
- Acrylamide is formed in coffee when coffee beans are roasted.
- Coffee is the largest source of acrylamide in the adult human diet.

Acrylamide

- The Margin of Exposure (MOE) is the point of comparison on the dose-response curve divided by the estimated intake by humans.
- It reflects the “margin” between exposure levels that harm animals and those to which people are exposed.
- A margin of exposure of 10,000 is considered “safe.”
- Acrylamide has a very low Margin of Exposure.
- According to the Joint FAO/WHO Expert Committee on Food Additives (JECFA), the MOE is just 75 to 300.
- According to the International Life Sciences Institute (ILSI), the MOE is just 40 to 160.
- People are exposed to acrylamide at levels that are just 100 times less than those that cause harm to experimental animals.
- According to WHO, this is a “major concern” to public health.

CERT's Interest

Council for Education and Research on Toxics

- The Council for Education and Research on Toxics (CERT) is a California public benefit corporation.
- CERT's charitable purposes are education and research regarding toxic substances.
- CERT is unique among NGOs because virtually every dollar that CERT receives is distributed as education and research grants.
- Most of CERT's funding for education and research has been grants to students and researchers at UC campuses.
- CERT has focused its attention on acrylamide, because acrylamide is the most prevalent carcinogen in the diet.

CERT's Interest in the Proposed Regulation

- CERT has long been in the vanguard of protecting Californians from acrylamide in the human diet.
- CERT filed the first case to enforce Proposition 65 regarding acrylamide in french fries in 2002.
- CERT co-litigated the next case regarding acrylamide in potato chips with the California Attorney General.
- In the french fry case, the manufacturers agreed to provide legally required cancer hazard warnings.
- In the potato chip case, the manufacturers agreed to reduce acrylamide so exposure would be below NSRL

Acrylamide-in-Coffee Case

- Since 2010 CERT has been litigating a case against the coffee industry regarding acrylamide in coffee -- *CERT v. Starbucks, et al.*, LASC No. BC 435759.
- Coffee is largest source of acrylamide in adult diet.
- The goal of the case is to persuade coffee roasters to reduce acrylamide levels in coffee.
- After 8 years of litigation, including two trials lasting a total of about 6 months, CERT prevailed in case.
- The proposed regulation appears to be a politically driven effort to overturn judge's decision in the case.

Acrylamide Can Be Reduced In Coffee

- The coffee industry can easily reduce acrylamide in coffee so NSRL for acrylamide will not be exceeded.
- Many techniques can reduce acrylamide levels in coffee without negatively affecting flavor or taste.
- This was the opinion of CERT's food science expert, Dr. Ronald Melnick, who testified about published and confidential industrial technologies at the trial.
- Just as the potato chip industry reduced acrylamide and maintained flavor & taste, so can coffee industry.
- Best result for public health – better than warnings.

European Commission Regulates Acrylamide in Coffee

- In 2017 the European Commission adopted Regulation 2017/2158, establishing measures and benchmark levels for the reduction of acrylamide in food, requiring Food Business Organizations to
- (1) identify the critical roast conditions to ensure minimal acrylamide formation within the target flavour profile;
- (2) incorporate control of roast conditions into a Pre-requisite Program as part of Good Manufacturing Practice and
- (3) consider the use of asparaginase treatment, insofar possible and effective to reduce the presence of acrylamide.

Coffee Industry Concealed Info From FDA

- FDA has not regulated acrylamide levels in coffee.
- The FDA was going to regulate acrylamide, but the coffee industry claimed that acrylamide could not be reduced in coffee without negatively affecting flavor.
- Nestle, one of the largest coffee roasters in the world, met with the FDA to address acrylamide in coffee.
- Nestle intentionally concealed info from the FDA that acrylamide could, in fact, be reduced in coffee.
- This is shown by a confidential Nestle memo that the judge in *CERT v. Starbucks* ordered declassified.

The "Smoking Gun" Document

1.1 Our Visit to the FDA was succesiful in influencing the FDA to use the tool box approach and against setting guidance values. Nega Beru at the FDA mentioned that FDA was going to issue a guidance document for the management of acrylamide which was not issued. We initially had offered to provide more data on Acrylamide to the FDA but on the advice of legal and of Nancy Rachman at GMA we were advised not to provide more data to the FDA because of the risk of the data being discovered in the event of a law suit under Prop 65.

Warning Required for Acrylamide in Coffee

2.1 The NSRL set for acrylamide as a carcinogen in California of 0.2 ug/day is so low that all our products will need a warning lable under Prop 65.

The Proposed Regulation

The Proposed Regulation

"Exposures to listed chemicals in coffee created by and inherent in the processes of roasting coffee beans or brewing coffee do not pose a significant risk of cancer."

Shortcomings of the Proposed Regulation

- The proposed regulation . . .
- does not consider that acrylamide is such a potent carcinogen that a cancer warning is required for all coffee.
- does not consider that acrylamide can be reduced in coffee without negatively affecting flavor and taste.

Contrary to OEHHA's Own Risk Assessment

- In 2005 OEHHA published an important report titled "Characterization of Acrylamide Intake from Certain Foods."
- In this report OEHHA evaluated whether consumption of coffee results in exposure to acrylamide above its No Significant Risk Level.
- In this report, OEHHA concluded:

Contrary to OEHHA's Own Risk Assessment

- "In all cases the lower bound on acrylamide intake (population-based intake) exceeded 1.0 µg/day. . . .
- "Based on the lower end of the range of consumption ... , average consumption of coffee with 4.1 ppb or more acrylamide concentration would exceed the NSRL. Since actual consumption by coffee drinkers is greater, a lower concentration would also exceed the . . . NSRL.
- "Of the individual brewed coffee samples tested by FDA, 19 of 20 had levels higher than 4.1 ppb.
- "All were above 1.9 ppb.
- "Thus, OEHHA is fairly confident that the NSRL is exceeded for coffee drinkers."

Doesn't Mention OEHHA's 2005 Determination

- Initial Statement of Reasons doesn't even mention the risk assessment OEHHA published in 2005.
- Bowing to political pressure from the coffee industry, OEHHA didn't even consider its own 2005 risk analysis that exposure to acrylamide in coffee exceeds the NSRL for all coffee drinkers – heavy, average, and light.
- Simply declaring that all heat-formed carcinogens in coffee pose no significant cancer risk is unscientific.
- Worse yet, the proposed regulation is contrary to OEHHA's own quantitative cancer risk assessment!

Reliance on IARC Monograph

OEHHA Misinterprets IARC Monograph

- From the Initial Statement of Reasons, it is clear that the major source of scientific information on which OEHHA relies is a Monograph published by the International Agency for Research on Cancer (IARC) regarding the carcinogenicity of coffee to humans.

- This Monograph was recently published, but reflects scientific research as of May 2016, when the Working Group on Coffee met in Lyon, France to evaluate coffee.

- OEHHA misinterprets IARC's conclusions in IARC's Monograph on Coffee in at least three critical respects.

OEHHA Misinterprets IARC Monograph

- First, OEHHA claims that "coffee has not been found to increase the risk of any cancers." [ISOR at p. 11]
- IARC never made any such conclusion.
- In fact, the IARC monograph reports significantly increased risks for a number of human cancers, especially childhood leukemia from maternal consumption of coffee during pregnancy.
- Significantly increased risks of cancer from consumption of coffee have also been reported for bladder cancer, esophageal cancer, gastric cancer, laryngeal cancer, lung cancer, non-Hodgkin's lymphoma, ovarian cancer, pancreatic cancer, prostate cancer, and total cancer.

OEHHA Misinterprets IARC Monograph

- Second, OEHHA assumes that inverse associations noted by IARC between coffee consumption and some cancers in observational studies are causal.
- IARC made no such determination.
- IARC concluded that “the available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence of a causal association between exposure and cancer.” [Preamble to the IARC Monograph]

OEHHA Misinterprets IARC Monograph

- Third, OEHHA claims that antioxidants in coffee prevent human cancer.
- IARC never made any such conclusion.
- The antioxidant-cancer prevention hypothesis is extremely controversial.
- Neither IARC nor any reputable scientific organization has ever concluded that antioxidants prevent human cancer.
- Meta-analyses of randomized controlled trials show that antioxidant intake actually causes some human cancers, rather than reducing human cancer.
- The mechanism by which antioxidants are hypothesized to prevent cancer (destruction of free radicals) is not relevant to the mechanism (genotoxicity and in particular clastogenicity) by which acrylamide causes cancer.

OEHHA Misinterprets IARC Monograph

- All 3 of OEHHA's conclusions misinterpret IARC:

- (1) IARC did not conclude that coffee consumption does not increase the risk of any human cancer.
- (2) IARC did not conclude that inverse associations between coffee and some cancers are causal.
- (3) IARC did not conclude that antioxidants in coffee prevent human cancer.

- OEHHA got it wrong on all three counts!!!

Post-IARC Studies Disprove That Coffee Prevents Cancer

Post-IARC Studies

- IARC completed its literature review in May 2016.
- At that time, the only epidemiological studies regarding coffee and cancer were observational studies.
- Observational epidemiology studies are not controlled studies – they are subject to much confounding and bias.
- Because of this, they cannot prove causation.
- This is especially true of nutritional epidemiology studies.
- Because observational nutritional epidemiology studies are scientifically inadequate to determine causation, and because the coffee-cancer epidemiology studies reported conflicting results, IARC concluded that coffee is *not classifiable* as to its carcinogenicity to humans.

Post-IARC Studies

- In the two years since IARC completed its review in May 2016, several epidemiology studies, specially designed to determine whether the inverse associations between coffee consumption and various chronic diseases (including cancer) are causal, have been published.
- These epidemiology studies used a sophisticated study design that is capable of determining causation.

Post-IARC Studies

- In the past two years, these special epidemiology studies have investigated causality of the inverse associations between coffee consumption and chronic diseases (type 2 diabetes, Alzheimer's disease, cardiovascular disease, Parkinson's disease) and cancer (prostate and ovarian).
- All of these studies – which post-date IARC's review – found no inverse association for coffee consumption and these diseases. In fact, some of them reported significantly increased risks of disease, including cancer.
- These studies provide strong scientific evidence that the inverse associations between coffee consumption and chronic diseases and cancer, as reported in observational studies, are not causal, but are instead artefactual.
- These studies show that the inverse associations for coffee and chronic diseases are likely due to confounding and reverse causation.
- Thus, these recent studies disprove the coffee-cancer prevention hypothesis!
- The Initial Statement of Reasons does not mention any of these important studies!

OEHHA'S Claim that Coffee is "Unique"

OEHHA's Claim That Coffee Is Unique

- OEHHA writes: "Coffee is unique in that it shows reductions in certain human cancers, has not been shown to increase any cancers, and is particularly rich in cancer chemo-preventive compounds." [Initial Statement of Reasons at page 11].

- This statement is scientifically incorrect, because the same is true of tobacco!

OEHHA's Claim That Coffee Is Unique

- Epidemiological studies of coffee consumption have reported decreased risks of breast cancer, endometrial cancer, melanoma, and thyroid cancer.
- This does not make coffee "unique" among chemical mixtures, because cigarette smoking has also been reported to reduce the risk of these same cancers.
- It is believed that smoking reduces the risk of these cancers, because cigarette smoke is anti-estrogenic.

OEHHA's Claim That Coffee Is Unique

- These studies don't mean that smoking is good for you.
- The positive association between coffee consumption and lung cancer is thought to be due to residual confounding by smoking, which is highly correlated with coffee consumption.
- Likewise, the negative association between coffee consumption and endometrial cancer is probably due to confounding by smoking.
- OEHHA failed to consider negative confounding by cigarette smoke as a biological explanation for the inverse association between coffee consumption and endometrial cancer. OEHHA incorrectly assumed that coffee consumption prevents endometrial cancer.

OEHHA's Claim That Coffee Is Unique

- OEHHA writes: "Coffee is unique in that it . . . is particularly rich in cancer chemopreventive compounds." [Initial Statement of Reasons at page 11].
- This statement is also erroneous, because the same is true of tobacco.
- "Tobacco . . . contains significant concentrations of polyphenols and carotenoids, which are important naturally occurring antioxidants." [Rodu B., "The Antioxidant Properties of Tobacco," *Tobacco Sci.* (2000) 44:71-73]
- "Major polyphenolics found in tobacco include chlorogenic acid, rutin, scopoletin and scopolen, along with . . . quercetin and kaempferol." [Leffingwell, "Basic Chemical Constituents of Tobacco Leaf and Differences among Tobacco Types," Chap. 8: Leaf Chemistry, in Davis DL et al., eds., *Tobacco: Production, Chemistry, and Technology* (Blackwell Science 1999)
- Thus, coffee is not unique because it is "particularly rich in cancer chemopreventive compounds." The same is true of the carcinogen tobacco!

OEHHA's Claim That Coffee Is Unique

- OEHHA also claims that coffee is unique because "it has been the subject of very high scientific interest for many years."
- This statement is likewise incorrect, because the same is also true of tobacco.
- Among complex chemical mixtures studied, coffee is surpassed only by tobacco, for which even more observational and experimental studies have been published than have been published regarding coffee.
- The most important analogy between coffee and tobacco is, of course, the addictive nature of these chemical mixtures, which arises from the reinforcing properties of caffeine and nicotine.
- OEHHA doesn't mention this important similarity between coffee and tobacco, instead relying on incorrect analogies for political reasons.

OEHHA'S Claim that Coffee is "Healthy"

OEHHA's Claim that Coffee is Healthy

- The Initial Statement of Reasons touts supposedly beneficial ("chemopreventive") chemicals in coffee.
- The Initial Statement of Reasons ignores the many carcinogenic and other toxic chemicals in coffee.
- Of the more than 1,000 chemicals in coffee, only about 50 have been evaluated for carcinogenicity in long-term bioassays.
- Of these, approximately two-thirds to three-fourths have shown carcinogenic activity in animals.

OEHHA's Claim that Coffee is Healthy

- Coffee contains caffeine.
- Caffeine, causes several adverse psychological and physiological effects, including medical disorders:
- caffeine intoxication,
- caffeine withdrawal syndrome,
- anxiety,
- sleep disorders, and
- problematic caffeine use.

OEHHA's Claim that Coffee is Healthy

- Because coffee is naturally bitter, it is typically consumed with sugars, sweeteners, creamers, whiteners, flavorings, and other additives.
- These additives are not healthy!
- They contain high levels of sugars and saturated fat, which are known to significantly increase the risk of cardiovascular diseases.
- Cardiovascular disease is a major risk factor for cancer.

OEHHA's Claim that Coffee is Healthy

- Coffee causes adverse pregnancy outcomes, including
- Reduced fetal weight and growth
- Pregnancy loss (including spontaneous abortion and stillbirth)
- Infertility (in both men and women)
- Adverse effects in children and adolescents.

OEHHA's Claim that Coffee is Healthy

- Consumption of coffee increases the risk of developing several chronic diseases:
- Bone disease (osteoporosis and fractures),
- Cardiovascular diseases (coronary heart disease, myocardial infarction, stroke, heart failure, and angina pectoris),
- Autoimmune diseases (rheumatoid arthritis, systemic lupus erythematosus, and type 1 diabetes),
- Gastrointestinal disorders (constipation, gallstones, and gastroesophageal reflux disease)
- Urological conditions (urolithiasis, lower urinary tract symptoms, urinary incontinence, and urinary tract infections)
- Acute cardiovascular events within 1 hour of consumption

OEHHA's Claim that Coffee is Healthy

- The Dietary Guidelines Advisory Committee Report does not prove the safety of coffee.
- Although this report suggests that coffee can be part of a healthy diet, the report also states that . . .
- Coffee should not be consumed by susceptible individuals (e.g. pregnant women, children),
- That it can be consumed by healthy people only "in moderation," and that
- "Individuals who do not consume caffeinated coffee should not start to consume it for health benefits …."

OEHHA's Claim that Coffee is Healthy

- That coffee has been consumed by millions of people for many years also does not establish safety.
- This is shown by the butter flavoring diacetyl, which the FDA classified as GRAS – Generally Recognized as Safe.
- The year that acrylamide was discovered in coffee, this food flavoring was found to be extremely toxic to the human respiratory system, causing a fatal lung disease in workers and consumers called "bronchiolitis obliterans."
- Significantly, this disease has been diagnosed in coffee roasting workers exposed to diacetyl in roasted coffee!

Legal Objections

Legal Objections

- The proposed regulation would contravene the intent of the Voters, who, in adopting Proposition 65, intended it to apply to carcinogens in coffee.
- Pre-election materials of both proponents and opponents of the Initiative asserted that the Act would apply to carcinogens in coffee.
- OEHHA therefore proposes to violate the intent of the electorate who, by a large majority, voted for Prop. 65.

Legal Objections

- The proposed regulation creates a categorical exemption for all listed heat-formed carcinogens in coffee in the absence of quantitative cancer risk assessments.
- Both Judge Ronald Robie (the trial court judge in the *Duke II* case) and Judge Elihu Berle (who tried the *CERT v. Starbucks* case), concluded that Proposition 65 does not allow any categorical exemptions from the warning requirement of Proposition 65 in the absence of a quantitative risk assessment showing the No Significant Risk Level for the listed carcinogen is not exceeded.
- The proposed regulation is therefore unlawful.

Legal Objections

- On December 23, 1992, a settlement agreement of the *Duke II* case was signed by Governor and the Health & Welfare Agency (OEHHA's predecessor).
- The settlement agreement provided "that any provision which is adopted after the date of this agreement to define the term 'no significant risk' of the Act for any food . . . shall be based upon specific numeric standards for the chemical . . . ."
- The proposed regulation therefore also violates the Settlement Agreement in the *Duke II* case.

Conclusions

Conclusions

- OEHHA's proposed regulation that would simply declare all listed heat-formed carcinogens in coffee to pose no significant risk of cancer – without any quantitative cancer risk assessment whatsoever – is grossly unscientific and wrong for many reasons.

Conclusions

- 1. The proposed regulation is inappropriate and unnecessary because the coffee industry can, and should, reduce acrylamide levels in coffee, so that coffee drinkers are not exposed to acrylamide from coffee in excess of the No Significant Risk Level.

Conclusions

- 2. The proposed regulation is contrary to OEHHA's own 2005 risk assessment, in which OEHHA concluded that all coffee drinkers are exposed to acrylamide in excess of the No Significant Risk Level.

Conclusions

- 3. The proposed regulation is based on OEHHA's erroneous interpretation of the IARC monograph. IARC did not conclude that coffee prevents cancer; it concluded that the available studies were inadequate to determine whether or not coffee causes cancer.

Conclusions

- 4. OEHHA's assertion that "coffee has not been found to increase the risk of any cancers" is incorrect. IARC found consistent epidemiologic evidence that maternal consumption of coffee during pregnancy significantly increases childhood leukemia. Many epidemiology studies have reported significantly increased risks of other cancers as well.

Conclusions

- 5. OEHHA's assumption that inverse associations between coffee consumption and cancers are causal is unfounded. IARC did not make such a conclusion, and OEHHA's assumption is contradicted by sophisticated new studies post-dating IARC's review.

Conclusions

- 6. OEHHA's assumption that antioxidants in coffee prevent cancer is unfounded. IARC made no such conclusion. OEHHA's assumption is contradicted by randomized controlled trials and meta-analyses of them which show no beneficial effect of antioxidant intake, but do show increased risks of some cancers.

Conclusions

- 7. OEHHA's claim that coffee is unique because it "is particularly rich in cancer chemo-preventive compounds" is unfounded. IARC made no such conclusion. OEHHA's assumption is erroneous, because "tobacco contains significant concentrations of polyphenols and carotenoids, which are important naturally occurring antioxidants." Tobacco also contains chlorogenic acids that are present in coffee.

Conclusions

- 8. OEHHA's claim that coffee is unique because it reduces the risk of certain cancers is incorrect. Just as consumption of coffee reduces the risk of endometrial cancer, thyroid cancer, and melanoma, tobacco smoke also reduces the risk of these cancers.

Conclusions

- 10. OEHHA's claim that coffee is unique because it "has been the subject of very high scientific interest for many years," is also incorrect. Among complex chemical mixtures, coffee is surpassed by tobacco, for which even more observational epidemiological studies have been published than coffee.

Conclusions

- 11. OEHHA's claim that coffee is healthy is incorrect. Coffee causes adverse physiological and psychological effects. Coffee also increases the risk of adverse reproductive and developmental effects and chronic diseases, including bone diseases, cardiovascular disease, autoimmune diseases, gastrointestinal diseases, and urological conditions.

Conclusions

- 12. The proposed regulation is unlawful because (1) it contradicts the intent of the Voters; (2) it creates a categorical exemption for carcinogens in coffee in the absence of any quantitative cancer risk assessment; (3) it contradicts OEHHA's own 2005 quantitative cancer risk assessment for exposure to acrylamide in coffee; and (4) it violates the state's agreement in settling the *Duke II* case "that any provision which is adopted after the date of this agreement to define the term 'no significant risk' of the Act for any food . . . shall be based upon specific numeric standards for the chemical."

Conclusions

- 13. OEHHA should not adopt the proposed regulation, but should instead withdraw the proposal, because it is contrary to science and law.

Conclusions

Thank you for your attention.